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FILE 'BIOSIS' ENTERED AT 18:38:35 ON 18 SEP 2004
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FILE 'MEDLINE' ENTERED AT 18:38:35 ON 18 SEP 2004

=> e Jeong JK/AU
E1            5     JEONG JIWON/AU
E2            2     JEONG JIYOON/AU
E3            0 --> JEONG JK/AU
E4            1     JEONG JOHN/AU
E5            2     JEONG JONG CHEOL/AU
E6            1     JEONG JONG DO/AU
E7            1     JEONG JONG HWA/AU
E8           12     JEONG JONG HYEON/AU
E9            8     JEONG JONG JIN/AU
E10           1     JEONG JONG KEUN/AU
E11           9     JEONG JONG MOON/AU
E12           1     JEONG JONG PIL/AU

=> s (hbv or hapatitis b virus)
L1        25549 (HBV OR HAPATITIS B VIRUS)

=> s (hbv-gfp)
L2            0 (HBV-GFP)

=> s (cis-acting)
L3        13972 (CIS-ACTING)

=> s l1 and l3
L4           70 L1 AND L3

=> s alpha
L5      1117572 ALPHA

=> s beta
L6      1135756 BETA

=> s l4 and l5 and l6
L7            0 L4 AND L5 AND L6

=> s l4 and l5
L8           10 L4 AND L5

=> s vector?
L9       287794 VECTOR?

=> s l8 and l9
L10           0 L8 AND L9

=> d l8 1-10 bib ab

L8   ANSWER 1 OF 10  BIOSIS  COPYRIGHT (c) 2004 The Thomson Corporation.  on
     STN
AN   1999:164681  BIOSIS
DN   PREV199900164681
TI   Hepatitis B virus-induced liver injury and altered expression of
     carcinogen metabolising enzymes: The role of the HBx protein.
AU   Chomarat, Pascale; Rice, Jerry M.; Slagle, Betty L.; Wild, Christopher P.
     [Reprint author]
CS   Mol. Epidemiol. Unit, Sch. Medicine, Algernon Firth Build., Univ. Leeds,
     Leeds LS2 9JT, UK
SO   Toxicology Letters (Shannon), (Dec. 28, 1998) Vol. 102-103, No. 0, pp.
     595-601. print.
     CODEN: TOLED5. ISSN: 0378-4274.
```

DT Article
LA English
ED Entered STN: 16 Apr 1999
Last Updated on STN: 16 Apr 1999
AB Hepatitis B virus (**HBV**) and aflatoxins are major risk factors for hepatocellular carcinoma (HCC) exhibiting a synergistic interaction in the development of this disease. The molecular mechanisms of this interaction remain to be elucidated but an altered carcinogen metabolism in the presence of hepatitis-induced liver injury is one hypothesis. The availability of biomarkers of aflatoxin exposure and metabolism permits this hypothesis to be examined in human populations whilst animal models, such as **HBV** transgenic mice permit parallel studies in an experimental setting. The hepatitis B virus X protein (HBx) is suspected to play a role in the hepatocarcinogenic process by virtue of its capacity to transactivate oncogenes and several other cellular genes via **cis-acting** elements. In previous studies in **HBV** transgenic mice expressing the HB surface antigen and X genes we observed a marked induction of specific cytochrome P450s (CYP) (Kirby et al., 1994a). In the current study we investigated the status of CYP, glutathione S-transferases (GST) and antioxidant enzymes in mice carrying only the X gene under the control of the **alpha**-1 antitrypsin regulatory elements (ATX mice). Livers of ATX mice showed no major pathological alterations compared to age-matched non-transgenic control mice. Immunohistochemical staining for CYP1A, 2A5 and GST expression and determination of related enzymatic activities (7-ethoxyresorufin O-deethylation, 7-methoxyresorufin O-deethylation, coumarin 7-hydroxylation and GST activities) revealed no differences between control and ATX mice. In addition, no differences in antioxidant enzymes were observed. Overall, these results support the conclusion that HBx expression alone is insufficient to induce transactivation of CYP and GST genes or to alter the antioxidant system and that the induction in other **HBV** models is a result of inflammatory injury in the liver, a feature absent in ATX mice. These data are compared to biomarker studies of enzyme activities in aflatoxin-exposed human populations with and without **HBV** infection.

L8 ANSWER 2 OF 10 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1997:486913 BIOSIS
DN PREV199799786116
TI Characterization of a specific region in the hepatitis B virus enhancer I for the efficient expression of X gene in the hepatic cell.
AU Fukai, Kenichi; Takada, Shinako; Yokosuka, Osamu; Saisho, Hiromitsu; Omata, Masao; Koike, Katsuro [Reprint author]
CS Dep. Gene Res., Cancer Inst., Kami-Ikebukuro, Toshima-ku, Tokyo 170, Japan
SO Virology, (1997) Vol. 236, No. 2, pp. 279-287.
CODEN: VIRLAX. ISSN: 0042-6822.
DT Article
LA English
ED Entered STN: 7 Nov 1997
Last Updated on STN: 7 Nov 1997
AB Hepatitis B virus (**HBV**) enhancer I has been shown to consist of several **cis-acting** sequences for the **HBV** gene expression efficiently in certain types of cells. Transcriptional regulation of **HBV** X gene mediated by enhancer I might be one of the mechanisms by which **HBV** obtains hepatotropism. By mutagenesis analysis of enhancer I function in the enhancer I/X gene promoter complex, we characterized a specific transcriptional regulatory region (designated as a LSR element, nt 989-1030) of enhancer I for the X gene promoter by means of the transient transfection technique using hepatic and nonhepatic cells. Based on the analysis of protein factors interacting with the LSR element, liver-enriched transcriptional factors, HNF3 and HNF4 or retinoid X receptor **alpha** (RXR-**alpha**), are probably implicated in the activity of enhancer I for the efficient

expression of X gene through their interaction with the LSR element in the hepatic cell. Furthermore, the isolated LSR element was demonstrated to function alone as a specific **cis-acting** element and to be able to activate transcription from the X gene promoter efficiently in the hepatic cell in an orientation-independent manner.

L8 ANSWER 3 OF 10 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1996:363988 BIOSIS
DN PREV199699086344
TI The hepatitis B virus posttranscriptional regulatory element is composed to two subelements.
AU Donello, John E.; Beeche, Arlyne A.; Iii, George J. Smith; Lucero, Ginger R.; Hope, Thomas J. [Reprint author]
CS Infectious Disease Laboratory, Salk Inst., P.O. Box 85800, San Diego, CA 92186-5800, USA
SO Journal of Virology, (1996) Vol. 70, No. 7, pp. 4345-4351.
CODEN: JOVIAM. ISSN: 0022-538X.
DT Article
LA English
ED Entered STN: 14 Aug 1996
Last Updated on STN: 14 Aug 1996
AB The RNAs of the hepatitis B virus (**HBV**) contain a **cis-acting** regulatory element which facilitates the cytoplasmic localization of unspliced transcripts (J. Huang and T. J. Liang, Mol. Cell. Biol. 13:7476-7486, 1993, and Z. M. Huang and T. S. Yen, J. Virol. 68:3193-3199, 1994). Such localization is presumed to be mediated by cellular factors which interact with the element. The **HBV** posttranscriptional regulatory element (HBVPRE) can efficiently activate an RNA export reporter system in an orientation-dependent and position-independent manner. Deletion analysis reveals that the HBVPRE consists of two subelements which function synergistically. A synergistic effect was also observed when the 5' (PRE-**alpha**) or 3' (PREP) subelements were duplicated. The bipartite structure of the HBVPRE is reminiscent of reports that the high-affinity binding sites of the Rev-like proteins must be duplicated to function efficiently (M. Grone, E. Hoffmann, S. Berchtold, B. R. Cullen, and R. Grassmann, Virology 204:144-152,1994; X. Huang, T. J. Hope, B. L. Bond, D. McDonald, K. Grahl, and T. G. Parslow, J. Virol. 65:2131-2134,1991; and D. McDonald, T. J. Hope, and T. G. Parslow, J. Virol. 66:7232-7238, 1992).

L8 ANSWER 4 OF 10 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1996:76964 BIOSIS
DN PREV199698649099
TI Cytokine inhibition of the hepatitis B virus core promoter.
AU Romero, Rene; Lavine, Joel E. [Reprint author]
CS Gastroenterol. and Nutrition, UCSD Med. Cent., San Diego, CA 92103-8450, USA
SO Hepatology, (1996) Vol. 23, No. 1, pp. 17-23.
CODEN: HPTLD9. ISSN: 0270-9139.
DT Article
LA English
ED Entered STN: 27 Feb 1996
Last Updated on STN: 27 Feb 1996
AB Hepatitis B virus (**HBV**) DNA contains consensus elements for transactivating proteins whose binding activity in other systems is regulated by inflammatory cytokines. Because **HBV** replicates within an environment of provoked inflammation, we speculated that the **HBV** core/pregenomic promoter may be regulated by cytokines produced in response to infection. To evaluate this hypothesis, the **HBV** core/pregenomic (C/P) promoter and associated **cis-acting** elements were placed upstream of a luciferase-encoding

plasmid. This reporter construct was transfected into cytokine-sensitive hepatoma cells permissive for **HBV** replication, which were exposed to stimulated mononuclear cell-conditioned medium or human recombinant cytokines. Conditioned medium reduced luciferase expression by 80%. Tumor necrosis factor **alpha** (TNF-**alpha**), interferon gamma (IFN-gamma), and interferon alfa (IFN-**alpha**) each reduced luciferase activity by 40%. Combinations of TNF-**alpha** and interferons mimicked the extent of conditioned medium inhibition. Nonspecific effects from diminished cellular viability or growth were not responsible for decreased luciferase activity. Retention of **HBV** DNA 330 basepairs upstream of the C/P transcription start site was required to maintain the TNF-**alpha** effect. A 60% reduction in **HBV** replicative forms within intracellular core particles was demonstrated with TNF-**alpha** treatment of Hep G2 cells stably transfected with **HBV** DNA. The inhibitory action of these cytokines implicates a noncytolytic mechanism by which antigen-nonspecific immune responses in part regulate **HBV** replication in infected hepatocytes. This function may be beneficial in accelerating viral clearance, but in alternative circumstances could contribute to viral persistence by attenuating immunogen recognition.

L8 ANSWER 5 OF 10 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1993:365306 BIOSIS
DN PREV199396050981
TI Functional interaction of nuclear factors EF-C, HNF-4, and RXR-**alpha** with hepatitis B virus enhancer I.
AU Garcia, Alonzo D.; Ostapchuk, Philomena; Hearing, Patrick [Reprint author]
CS Dep. Microbiol., Health Sci. Center, State Univ. New York, Stony Brook, NY 11794, USA
SO Journal of Virology, (1993) Vol. 67, No. 7, pp. 3940-3950.
CODEN: JOVIAM. ISSN: 0022-538X.
DT Article
LA English
ED Entered STN: 6 Aug 1993
Last Updated on STN: 6 Aug 1993
AB Hepatitis B virus (**HBV**) enhancer I contains **cis-acting** elements that are both sufficient and essential for liver-specific enhancer function. The EF-C binding site was previously shown to be a key element in enhancer I. EF-C binding activity is evident in hepatic and nonhepatic cells. Although the EF-C binding site is required for efficient **HBV** enhancer I function, the EF-C site does not possess intrinsic enhancer activity when assayed in the absence of flanking elements. We have defined a novel region in **HBV** enhancer I, termed the GB element, that is adjacent to and functions in conjunction with the EF-C binding site. The GB element and EF-C site confer interdependent liver-specific enhancer activity in the absence of flanking **HBV** enhancer sequences. The nucleotide sequence of the GB element is similar to sequences of the DNA binding sites for members of the steroid receptor superfamily. Among these proteins, we demonstrate that HNF-4, RXR (retinoid X receptor), and COUP-TF bind to the GB element in vitro. HNF-4 transactivates a promoter linked to a multimerized GB/EF-C domain via the GB element in vivo in a manner that is dependent on the integrity of the adjacent EF-C binding site. RXR-**alpha** also transactivates promoter expression via the GB element in vivo in response to retinoic acid but in a largely EF-C-independent manner. Finally, we show that COLT-TF antagonizes the activity of the GB element in human liver cells.

L8 ANSWER 6 OF 10 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1992:500330 BIOSIS
DN PREV199294118855; BA94:118855
TI EFFECT OF CYTOKINES AND OTHER FACTORS ON THE PRES1 AND PRES2 PROMOTER

ACTIVITIES OF THE HEPATITIS B VIRUS SUBTYPE ADR.
AU LEE Y S [Reprint author]
CS DEP INTERNAL MED, CATHOLIC UNIV MED COLL, SEOUL, KOREA
SO Journal of Catholic Medical College, (1992) Vol. 45, No. 2, pp. 491-499, 501-502.
CODEN: KTUNAA. ISSN: 0368-7015.
DT Article
FS BA
LA KOREAN
ED Entered STN: 9 Nov 1992
Last Updated on STN: 9 Nov 1992
AB Expression of PreS1/PreS2/S gene is regulated by complex interplay between regulatory sequences in the PreS1 and PreS2 promoters and many other positive and negative elements, such as viral enhancers, **cis-acting** element in the HBx gene, cellular transcription factors. Although the exact mechanisms that regulate expression of surface antigen genes are not clear, cell line specificity and subtype specificity were observed by many studies which used adw and ayw subtypes, that are not common in Korea. The DNA fragments of the PreS1 and PreS2 promoters were amplified from the **HBV** DNA (subtype adr) which were isolated from a Korean HBsAg carrier by polymerase chain reaction (PCR). Oligonucleotides which contains either Hind III or Xba I recognition sites on their 5' ends or 3' ends respectively were generated by oligonucleotide synthesizer and they were used as primers for PCR. After ligating these DNA fragments into chloramphenicol acetyl transferase (CAT) reporter gene, the promoter activities were analyzed by transient transfection assays. The influences of cytokines, oncogenes, tumor suppressor gene, viral transactivators and transcription factor on the activities of PreS1 and PreS2 promoters were screened by CAT assays. While Ras, Src, E7, SV40T and AP-2 increased the PreS1 and PreS2 promoter activities, tumor necrosis factor .**alpha**. was shown to inhibit these promoter activities.

L8 ANSWER 7 OF 10 MEDLINE on STN
AN 1999144917 MEDLINE
DN PubMed ID: 10022319
TI Hepatitis B virus-induced liver injury and altered expression of carcinogen metabolising enzymes: the role of the HBx protein.
AU Chomarat P; Rice J M; Slagle B L; Wild C P
CS Unit of Environmental Carcinogenesis, International Agency for Research on Cancer, Lyon, France.
NC CA54557 (NCI)
ES06052 (NIEHS)
SO Toxicology letters, (1998 Dec 28) 102-103 595-601.
Journal code: 7709027. ISSN: 0378-4274.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199902
ED Entered STN: 19990311
Last Updated on STN: 19990311
Entered Medline: 19990225
AB Hepatitis B virus (**HBV**) and aflatoxins are major risk factors for hepatocellular carcinoma (HCC) exhibiting a synergistic interaction in the development of this disease. The molecular mechanisms of this interaction remain to be elucidated but an altered carcinogen metabolism in the presence of hepatitis-induced liver injury is one hypothesis. The availability of biomarkers of aflatoxin exposure and metabolism permits this hypothesis to be examined in human populations whilst animal models, such as **HBV** transgenic mice permit parallel studies in an experimental setting. The hepatitis B virus X protein (HBx) is suspected to play a role in the hepatocarcinogenic process by virtue of its capacity to transactivate oncogenes and several other cellular genes via **cis-acting** elements. In previous studies in **HBV**

transgenic mice expressing the HB surface antigen and X genes we observed a marked induction of specific cytochrome P450s (CYP) (Kirby et al., 1994a). In the current study we investigated the status of CYP, glutathione S-transferases (GST) and antioxidant enzymes in mice carrying only the X gene under the control of the **alpha**-1 antitrypsin regulatory elements (ATX mice). Livers of ATX mice showed no major pathological alterations compared to age-matched non-transgenic control mice. Immunohistochemical staining for CYP1A, 2A5 and GST expression and determination of related enzymatic activities (7-ethoxyresorufin O-deethylation, 7-methoxyresorufin O-deethylation, coumarin 7-hydroxylation and GST activities) revealed no differences between control and ATX mice. In addition, no differences in antioxidant enzymes were observed. Overall, these results support the conclusion that HBx expression alone is insufficient to induce transactivation of CYP and GST genes or to alter the antioxidant system and that the induction in other **HBV** models is a result of inflammatory injury in the liver, a feature absent in ATX mice. These data are compared to biomarker studies of enzyme activities in aflatoxin-exposed human populations with and without **HBV** infection.

L8 ANSWER 8 OF 10 MEDLINE on STN
AN 97467761 MEDLINE
DN PubMed ID: 9325235
TI Characterization of a specific region in the hepatitis B virus enhancer I for the efficient expression of X gene in the hepatic cell.
AU Fukai K; Takada S; Yokosuka O; Saisho H; Omata M; Koike K
CS Department of Gene Research, Cancer Institute, JFCR, Tokyo, Japan.
SO Virology, (1997 Sep 29) 236 (2) 279-87.
Journal code: 0110674. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199711
ED Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971106
AB Hepatitis B virus (**HBV**) enhancer I has been shown to consist of several **cis-acting** sequences for the **HBV** gene expression efficiently in certain types of cells. Transcriptional regulation of **HBV** X gene mediated by enhancer I might be one of the mechanisms by which **HBV** obtains hepatotropism. By mutagenesis analysis of enhancer I function in the enhancer I/X gene promoter complex, we characterized a specific transcriptional regulatory region (designated as a LSR element, nt 989-1030) of enhancer I for the X gene promoter by means of the transient transfection technique using hepatic and nonhepatic cells. Based on the analysis of protein factors interacting with the LSR element, liver-enriched transcriptional factors, HNF3 and HNF4 or retinoid X receptor **alpha** (RXR **alpha**), are probably implicated in the activity of enhancer I for the efficient expression of X gene through their interaction with the LSR element in the hepatic cell. Furthermore, the isolated LSR element was demonstrated to function alone as a specific **cis-acting** element and to be able to activate transcription from the X gene promoter efficiently in the hepatic cell in an orientation-independent manner.

L8 ANSWER 9 OF 10 MEDLINE on STN
AN 96133438 MEDLINE
DN PubMed ID: 8550037
TI Cytokine inhibition of the hepatitis B virus core promoter.
AU Romero R; Lavine J E
CS Combined Program in Pediatric Gastroenterology and Nutrition, Children's Hospital, Boston, MA, USA.
NC DK08771-03 (NIDDK)

PO1DK33506-09 (NIDDK)
SO Hepatology (Baltimore, Md.), (1996 Jan) 23 (1) 17-23.
Journal code: 8302946. ISSN: 0270-9139.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199602
ED Entered STN: 19960306
Last Updated on STN: 19970203
Entered Medline: 19960220
AB Hepatitis B virus (**HBV**) DNA contains consensus elements for transactivating proteins whose binding activity in other systems is regulated by inflammatory cytokines. Because **HBV** replicates within an environment of provoked inflammation, we speculated that the **HBV** core/pregenomic promoter may be regulated by cytokines produced in response to infection. To evaluate this hypothesis, the **HBV** core/pregenomic (C/P) promoter and associated **cis-acting** elements were placed upstream of a luciferase-encoding plasmid. This reporter construct was transfected into cytokine-sensitive hepatoma cells permissive for **HBV** replication, which were exposed to stimulated mononuclear cell-conditioned medium or human recombinant cytokines. Conditioned medium reduced luciferase expression by 80%. Tumor necrosis factor **alpha** (TNF-**alpha**), interferon gamma (IFN-gamma), and interferon alfa (IFN-**alpha**) each reduced luciferase activity by 40%. Combinations of TNF-**alpha** and interferons mimicked the extent of conditioned medium inhibition. Non-specific effects from diminished cellular viability or growth were not responsible for decreased luciferase activity. Retention of **HBV** DNA 330 basepairs upstream of the C/P transcription start site was required to maintain the TNF-**alpha** effect. A 60% reduction in **HBV** replicative forms within intracellular core particles was demonstrated with TNF-**alpha** treatment of Hep G2 cells stably transfected with **HBV** DNA. The inhibitory action of these cytokines implicates a noncytolytic mechanism by which antigen-nonspecific immune responses in part regulate **HBV** replication in infected hepatocytes. This function may be beneficial in accelerating viral clearance, but in alternative circumstances could contribute to viral persistence by attenuating immunogen recognition.

L8 ANSWER 10 OF 10 MEDLINE on STN
AN 93287211 MEDLINE
DN PubMed ID: 8389913
TI Functional interaction of nuclear factors EF-C, HNF-4, and RXR **alpha** with hepatitis B virus enhancer I.
AU Garcia A D; Ostapchuk P; Hearing P
CS Department of Microbiology, State University of New York, Stony Brook 11794.
NC AI29427 (NIAID)
CA44673 (NCI)
SO Journal of virology, (1993 Jul) 67 (7) 3940-50.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199307
ED Entered STN: 19930723
Last Updated on STN: 19990129
Entered Medline: 19930712
AB Hepatitis B virus (**HBV**) enhancer I contains **cis-acting** elements that are both sufficient and essential for liver-specific enhancer function. The EF-C binding site was previously shown to be a key element in enhancer I. EF-C binding activity is evident

in hepatic and nonhepatic cells. Although the EF-C binding site is required for efficient **HBV** enhancer I function, the EF-C site does not possess intrinsic enhancer activity when assayed in the absence of flanking elements. We have defined a novel region in **HBV** enhancer I, termed the GB element, that is adjacent to and functions in conjunction with the EF-C binding site. The GB element and EF-C site confer interdependent liver-specific enhancer activity in the absence of flanking **HBV** enhancer sequences. The nucleotide sequence of the GB element is similar to sequences of the DNA binding sites for members of the steroid receptor superfamily. Among these proteins, we demonstrate that HNF-4, RXR (retinoid X receptor), and COUP-TF bind to the GB element in vitro. HNF-4 transactivates a promoter linked to a multimerized GB/EF-C domain via the GB element in vivo in a manner that is dependent on the integrity of the adjacent EF-C binding site. RXR **alpha** also transactivates promoter expression via the GB element in vivo in response to retinoic acid but in a largely EF-C-independent manner. Finally, we show that COUP-TF antagonizes the activity of the GB element in human liver cells.